

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1, 8-15, 17-20 and 23-25 are pending. The amendments are supported by the original disclosure and, thus, no new matter is added by their entry.

35 U.S.C. 112 – Enablement

Claims 1-25 and 40-42 were rejected under Section 112, first paragraph. It was alleged, “The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.” Applicants traverse because the claims as amended are directed to a transgenic mouse comprising disruption of the gene(s) encoding melusin. Note that the Examiner alleges that a homozygous disruption is required to obtain the observed phenotype. This is incorrect. The melusin gene is located on the X chromosome. Therefore, depending on the gender of the transgenic mouse, the melusin gene is disrupted in one or two copies.

A female mouse has two copies of the melusin gene; a male mouse has only one copy of the melusin gene. A single disrupted gene in a transgenic male mouse would have a phenotype. But even a transgenic female mouse bearing a single disrupted gene has utility because she is a carrier for the phenotype. In a female, one X chromosome in each somatic cell is randomly inactivated. Therefore, depending on the natural effect of this form of gene inactivation, the transgenic female mouse also is chimeric for cells that are inactivated for melusin gene function even in the heterozygous state.

Withdrawal of the enablement rejection is requested because it would not require undue experimentation for the skilled person to make and use the claimed invention.

35 U.S.C. 112 – Definiteness

Claims 8 and 10-11 were rejected under Section 112, second paragraph, as being allegedly “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Applicants traverse because the claims are amended as suggested by the Examiner.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 103 – Nonobviousness

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See *id.* at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case of obviousness under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn*, 78 USPQ2d at 1335; see *KSR*, 82 USPQ2d at 1396. An inquiry should be made as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* at 1396. But a claim which is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 1396. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 1-6, 15-16, 20-22 and 24-25 were rejected under Section 103(a) as allegedly unpatentable over Brancaccio et al. (J. Biol. Chem. 274:29282-29288, 1999) in view of Flatschart & Sogayar (Brazilian J. Med. Biol. Res., 32:867-875, 1999) and

Capecchi (Trends Genet. 5:70-76, 1989). Applicants traverse because the combination proposed in the Office Action is a mere invitation to experiment. The line of investigation that is suggested by the Examiner to be obvious would be performed with no definite objective and lacks utility: i.e., making a transgenic mouse comprising a disruption in its melusin gene to determine the biological role of melusin (see pages 26-27 of the Office Action). One of ordinary skill in the art would be making transgenic mice with no idea of what phenotype would be expected, or even whether there would be an observable effect at the end of these extensive line of experiments.

The cited document lack any teaching or suggestion of a specific biological role of melusin in physiology. By contrast, Applicants' specification teaches and the pending claims require that the transgenic mouse has a phenotype (e.g., impaired heart hypertrophy, heart dilation, heart failure) after being subjected to a hypertensive condition. Such specific biological functions of melusin are unexpected results of the invention. No rationale is presented in the Office Action for making the invention *prima facie* obvious. It is clearly "more than the predictable use of prior art elements according to their established functions" and the prior art does not establish "a reasonable expectation of success" to make the claimed invention.

Claims 1-4, 15 and 20 were rejected under Section 103(a) as allegedly unpatentable over Brancaccio et al. in view of Ignelzi et al. (Crit. Rev. Oral Biol. Med. 6:181-201, 1995). Applicants traverse because the combination proposed in the Office Action is a mere invitation to experiment. The line of investigation that is suggested by the Examiner to be obvious would be performed with no definite objective and lacks utility: i.e., making a transgenic mouse comprising a disruption in its melusin gene to determine the biological role of melusin (see pages 26-27 of the Office Action). One of ordinary skill in the art would be making transgenic mice with no idea of what phenotype would be expected, or even whether there would be an observable effect at the end of these extensive line of experiments.

The cited document lack any teaching or suggestion of a specific biological role of melusin in physiology. By contrast, Applicants' specification teaches and the pending claims require that the transgenic mouse has a phenotype (e.g., impaired heart hyper-

trophy, heart dilation, heart failure) after being subjected to a hypertensive condition. Such specific biological functions of melusin are unexpected results of the invention. No rationale is presented in the Office Action for making the invention prima facie obvious. It is clearly “more than the predictable use of prior art elements according to their established functions” and the prior art does not establish “a reasonable expectation of success” to make the claimed invention.

Withdrawal of the Section 103 rejections is requested because the claimed invention would not have been obvious to the ordinarily skilled artisan at the time Applicants made their invention.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /Gary R. Tanigawa/
Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100